REMARKS

The present invention is directed to new dosage forms of atorvastatin that solve the degradation problems associated with the atorvastatin formulations of the prior art. Claim 1 has been amended as will be discussed below. Claims 2-7, 13-16, and 18-30 have been cancelled. New claims 31-38 have been added. It is respectfully submitted that the claims are in condition for allowance. Reconsideration is respectfully requested.

REJECTION UNDER 35 USC 112

Claim 1, and the remaining claims depending from it, was rejected under the second paragraph of 35 USC 112 due to an improper Markush group. It is respectfully submitted that this rejection is moot in view of the amendments to claim 1.

Double Patenting Objection

The claims were also provisionally rejected on the grounds of non-statutory obviousness-type double patenting in view of co-pending United States patent applications 10/828,398 and 10/828,079. It is respectfully submitted that this rejection is moot in view of the attached terminal disclaimer.

Rejection under 35 USC 103

Claims 1, 2, 4, 6-12, 14, 15, and 17 were rejected under 35 USC 103 as being unpatentable over Wilson et al in view of Kerc et al. It is respectfully submitted that the amendments to claim 1 overcomes this rejection and that the claims define over the art and are in condition for allowance.

The USPTO is relying upon Wilson et al as the primary reference. The USPTO has asserted that Wilson et al discloses the production of atorvastatin dosage forms prepared without a granulation step, containing less than 5% of an alkaline earth metal. To support this position the USPTO cites Examples 1-39 of Wilson et al.

This is factually incorrect. Wilson et al's disclosure is much more limited. Wilson et al's disclosure is limited to liquid and semi-solid dosage forms. While Wilson

fails to define semi-solid, this term typically refers to a "viscous slowly flowing substance" (see www.yourdictionary.com/semissolid). At www.toolingu.com, a semi-solid is defined as "a substance that has a gel-like mixture and is not classified as a fluid or solid. Industrial grease is classified as a semi-solid."

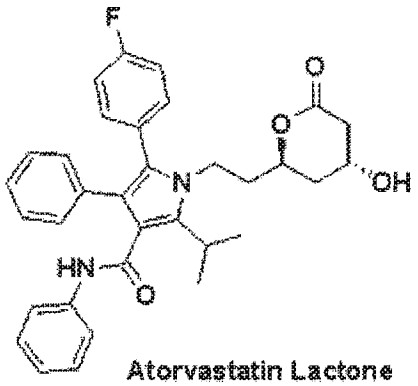
Further Wilson et al does not specifically disclose the preparation of an atorvastatin dosage form, or any other statin. On page 5, beginning at line 5, Wilson et al states that his formulation may be utilized for any chemical containing "an acid". Examples of such substances include non-steroidal inflammatory agents, histamine H1 receptor antagonists, mast cell stabilizers such as cromlyn, inhibitors of gastric acid secrtion such as omeprazole, antihyperlipidemia agents such as gemfibrozil, antibiotics such as penicillin, cephlasporins, and fluoroquinolines, anti-acne drugs, prostaglandins, hypolipemics, and finally statins, such as atorvastatin.

In the thirty nine examples, Wilson specifically discloses the preparation of a number liquids and gels containing non-steroidal agents such as diclofenac, sulindac, indomethacin, etc. Not one of the examples discloses an atorvastatin formulation, or any other statin. As will be discussed further below, Wilson et al and Applicants were focused upon solving entirely different problems.

Claim 1 has been amended to further differentiate the claims from Wilson et al. Claim 1 now specifies that the atorvastatin formulation must be a tablet. Further this tablet is produced by direct compression. Support for this amendment may be found on page 11 of the specification and in the Examples, more specifically in Example 4.

This distinction is not merely a matter of semantics. Wilson et al and Applicants were focusing upon entirely different problems. Wilson et al was attempting to produce dosage forms that decreased the incidence of gastric irritation typically associated with non-steroidal anti-inflammatory agents (see pages 1 and 4).

By contrast, Applicants were attempting to solve the problems associated with the chemical degradation of solid atorvastatin. As is discussed on pages 12-14 of the specification, solid atorvastatin is subject to chemical degradation when stored under ambient conditions. Atorvastatin is converted to atorvastatin lactone as shown below.



Atorvastatin Lactone

As is discussed beginning at page 5 of Applicants specification, the prior art teaches that substantial quantities of bases, such as alkaline earth metals, must be incorporated into an atorvastain formulation to prevent formation of the lactone.

As is discussed on page 12 of Applicants' specification, beginning at line 30, Applicants discovered that formation of atorvastatin lactone, in solid dosage forms, can be avoided if the granulation step is omitted. Replacement with direct compression is one suitable solution. Omitting the granulation step also allows elimination of alkaline earth metals and other basic substances.

The secondary reference, Kerc et al, also discusses the chemical instability associated with atorvastatin (see page 3, lines 7-23). Kerc et al's solution is also to incorporate bases into the formulation to inhibit the formation of atorvastatin lactone. Kerc et al provides no suggestion that omitting the granulation step could solve this lactonization problem. A review of all the examples and comparative examples of Kerc et al shows they were prepared using a granulation step. None of the examples omit this granulation step.

A review of the Kerc et al's examples also shows that substantial quantities of base, well in excess of the 5 w/w% specified in claim 1, were routinely used. In Example 1, on page 14, Kerc et al uses magnesium oxide to stabilize the formulation. It was present in the quantity of 10.4 w/w%. In example 2, sodium phosphate is the base and is present in the quantity of 45 w/w%. Similar results are depicted in Examples 3-6 on pages 15 of Kerc et al. Kerc et al did describe two comparative experiments, on pages 7

and 8, in which the bases were omitted from the formulation. Kerc et al concludes that these formulations were inferior due to the limited amount of atorvastatin found in the media after dissolution.

In summary, claim 1 has been amended to differentiate it from Wilson et al and Kerc et al. Claim 1 now specifies that the formulation must be a tablet produced via direct compression. Wilson is directed to liquids and gels. Direct compression is irrelevant to the production of such dosage forms. Kerc et al does not address this deficiency. All of the formulations of Kerc et al were produced via a granulation step. Further, Kerc et al emphasizes the need to incorporate substantial quantities of bases into atorvastin formulations to provide both acceptable stability and dissolution. Kerc et al teaches away from the solution embodied by pending claim 1.

Withdrawal of the rejections of record and reconsideration is respectfully requested. If the USPTO feels that minor amendments are required to place the case in condition for allowance, the undersigned invites a phone call to discuss such proposals.

A prompt and favorable response is earnestly solicited.

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